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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,905	04/24/2000	TOHRU TANI	FJN-077	7282

7590 04/22/2002

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	14

DATE MAILED: 04/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/423,905	Tani et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 17, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *2-23* is/are pending in the application.

4a) Of the above, claim(s) *12 and 23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *2-11 and 13-22* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *2-23* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The response filed 1-17-02 has been entered into the record.

Drawings

2. The drawings are objected to for reasons set forth on the PTO-498 attached hereto. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

3. The information disclosure statement filed 7-18-00 fails to fully comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because copies of the crossed out references on page 4 of the IDS were not provided and the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Election/Restriction

4. Applicant's election of Group I (Claims 2-11 and 13-22) in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 12 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Claim Rejections - 35 U.S.C. § 112

6. Claims 4 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 4 and 15, are directed to the concept of administering the TCF-II protein by administering a recombinant host cell. The specification as originally filed does not provide conception of cell based therapeutic agents. This matter is best resolved by Applicants pointing to the specification by page and line number were conception of the claimed invention can be found.

7. Claims 2-11 and 13-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the survival rate of sepsis in a mammal by decreasing lipopolysaccharide (LPS)-induced bacterial translocation in the intestine comprising administering to the mammal an amount of isolated or purified tissue cytotoxic factor - II (TCF-II) sufficient to decrease LPS-induced bacterial translocation in the intestine thereby increasing the survival rate of sepsis, it does not reasonably provide enablement for unpurified TCF-II, all aspects of treatment of sepsis, all types of sepsis, cell therapy, prevention of sepsis or use of polysaccharide chains or variants thereof. The specification does not enable any person skilled in the art to which

it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As to claims 2-11 and 13-22, the teachings of the specification are limited to the administration of purified TCF-II to increase the survival rate of septic mammals by means of decreasing LPS-induced bacterial translocation in the intestine. The state of the art with respect to treatment of sepsis is complicated because sepsis is a toxic condition relating to the spread of bacteria or their toxic products from a focus of infection. Toxic symptomatic conditions associated with sepsis are fever, chills, tachycardia, and somnolence. In the further course septic shock with bacteremia, thrombocytopenia, circulatory breakdown, and failure of multiple organs may occur. Sepsis may occur with many different types of microorganisms (fungi, gram positive and gram negative) and have different foci of infection (prosthesis, blood, skin, catheters of various types). The specification does not teach the effect of TCF-II on any of these symptomatic parameters associated with sepsis, nor bacterial growth or translocation in sepsis associated with other foci of infection. Further, the specification does not teach prevention of all mortality and morbidity (i.e. fever, chills) and that administration of TCF-II is unable to prevent either sepsis or death due to LPS-mediated bacterial translocation of the intestine. Figure 1, teaches that after 2 days of treatment only 9 out of 11 animals remained alive, some of the animal succumbed to sepsis at day 2, a clear indication that sepsis and infection can not be prevented. Further evidence that sepsis can not be prevented is clearly established by the specification that teaches that treatment with TCF-II subsequent to puncture of the cecum still provided for infection and travel of the infection from the locus (intestine) to the mesenteric lymph node (see Figure 1, Example 2). Administration of TCF-II can clearly not prevent infection and thereby prevent sepsis.

To complicate the issue, sepsis can occur by other means (i.e. blood transfusion, urogenital, prosthetic devices) and even if LPS-induced bacterial translocation of bacterial across the intestine could be totally ablated, then all types of sepsis still could not be prevented because sepsis can be induced by infection from other foci (i.e. skin, urogenital, prosthesis) which have not been demonstrated to be effected by administration of TCF-II. Additionally, the microorganisms derived from these other sources do not necessarily have LPS and as such would not be amenable to treatment by means of prevention of translocation. Since, the claims include sepsis induced by means other than LPS-mediated bacterial translocation across the intestine that has not been found to be treatable by TCF-II, the claims in regard to this scope are not enabled.

As to claims 4 and 15, the claims recite the administration of cells producing TCF-II. The specification provides no written description of how cells producing TCF-II would be administered and how to deliver the cells to focus of infection in sufficient amounts to treat or prevent sepsis.

As to claims 11 and 12, the specification and the fails to teach the exact chemical structure of any polysaccharide chains attached to native or recombinant TCF-II . as result, the specification fails to provide any written description of how to modify any polysaccharide chain attached to TCF-II, native or otherwise, to achieve a functional therapeutic. There is no guidance in this specification of how to modify the polysaccharide side chain. There is no starting point for variation and no description of how to achieve a polysaccharide chain variant. The specification has no apparent description of how to make and use polysaccharides. Applicants are invited to point to the page and line number in the specification where written description can be found for how to make and use these polysaccharides. While the courts have that a patent need not teach, and preferably

omits, what is well known in the art. The omission of all details of how to make and use the product can not constitute an enabling specification. Reliance on the skill of the art would not be persuasive to remove this rejection because; as also recognized by the Federal Circuit:

> "However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material *or of any conditions under which a process can be carried out,* [emphasis added] undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research." (Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001).

In the instant case there is no disclosure of any conditions under which the polysaccharide chains or variants thereof can be made and used. The specification is apparently devoid of any description of how to make and use such polysaccharides. As such, the failure of this specification of how to make and use the polysaccharides or variants thereof constitutes undue experimentation.

In view of the limited teachings of the specification, the breadth of the claimed subject matter as it relates to the symptoms of sepsis, the different organisms that cause sepsis, the generation of sepsis by different routes, the unpredictability of the treatment of each or the lack of showing of prevention of sepsis, the lack of teaching of how to use unpurified TCF-II, the lack of teaching as to how to use cells expressing TCF-II, the lack of teaching of how to make polysaccharides or functional variants, one of skill in the art

would be forced into undue experimentation to make and use the TCF-II variants, cells or polysaccharides of the claimed invention to treat all aspects of sepsis.

8. Claims 2-11 and 13-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 2-11 and 13-22, the recitation of the acronym TCF-II is indefinite, while acronyms are permitted in the claims, the first appearance of the acronym should be preceeded by it full name. Amendment of the claim to rectite tissue cytotoxic factor -II (TCF-II) would obviate this rejection.

As to claims 2-11, the term "treatment" is indefinite as it relates to sepsis because it is unclear what aspects of sepsis are being treated. For example, sepsis includes fever, chills, tachycardia, somnolence, bacteremia, thrombocytopenia, circulatory breakdown, and failure of multiple organs. As such, it is unclear as to what aspects of sepsis are being treated.

As to claims 11 and 22, TCF-II is described in the specification as a polypeptide. The instant claims are confusing because they apparently redefine TCF-II as a polysaccharide chain and consequently, the metes and bounds of the claimed subject matter can not be ascertained.

Claim Rejections - 35 U.S.C. § 102 or 103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 2-11 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/41230 (Reference BO on PTOL-1449) or WO98/40096 (Reference BP on PTOL-1449).

These references are applied as intervening prior art because the priority document is not in English. Submission of a certified English translation of the Japanese priority document may overcome these rejections.

WO 98/41230 teaches administration of TCF-II for infectious disease and endotoxinemia. Endotoxinemia is a parameter of sepsis. WO 98/41230 teaches the administration of TCF-II in the same dosages recited herein: 0.6-600 mg/day or 6-60 mg/day in a pH conditioner, buffer and/or stabilizer (see page 7 of the translation). WO 98/41230 contemplates the use of recombinant TCF-II (pages 8-9). As such, the administration of the TCF-II to patients with endotoxinemia would inherently treat sepsis.

WO 98/40096 teaches administration of TCF-II for multiple organ failure. Multiple organ failure is an associated parameter of sepsis. WO 98/40096 teaches the administration of TCF-II in the same dosages recited herein: 0.6-600 mg/day or 6-60 mg/day in a pH conditioner, buffer and/or stabilizer (see page 7 of the translation). WO 98/40096 contemplates the use of recombinant TCF-II (pages 8-9). As such, the administration of the TCF-II to patients with multiple organ failure would inherently treat sepsis.

Status of Claims

11. No claims are allowed.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should

applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
April 20, 2002

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600